

Intrathecal Sufentanil for Labor Analgesia Does Not Cause a Sympathectomy

Edward T. Riley, M.D.,* Dean Walker, M.D.,† Catherine L. Hamilton, M.D.,‡ Sheila E. Cohen, M.B., Ch.B.‡

Background: Intrathecal sufentanil (ITS) is frequently used to provide analgesia during labor. Decreases in blood pressure and sensory changes in this circumstance suggest that ITS may have a local anesthetic effect and thus cause a sympathectomy. To determine whether ITS given to laboring women causes a sympathectomy, the authors evaluated central and lower extremity temperature changes after ITS administration. These findings were compared with those in a control group of women having spinal anesthesia with bupivacaine for elective cesarean section in whom an extensive sympathectomy was expected.

Methods: Twenty parturients classified as American Society of Anesthesiologists' physical status 1 or 2 had temperatures measured centrally, at the calf, and at the great toe at frequent intervals after receiving 10 µg ITS for labor analgesia (sufentanil group, n = 10), or hyperbaric bupivacaine 12 mg in their spinal anesthetic for cesarean section (bupivacaine group, n = 10). Calf-to-toe temperature indices (C-T) were calculated by subtracting toe temperature from calf temperature. A decrease in this index means that the toe had warmed compared with the calf and is an indication of vasodilation and a sympathectomy.

Results: There was no significant change in the C-T indices or central temperature in the sufentanil group, but the C-T indices and central temperature decreased significantly in the bupivacaine group.

Conclusions: The decreases in the C-T index and central temperature in the bupivacaine group indicate the presence of a sympathectomy. The lack of change in the C-T indices and central temperature in the sufentanil group indicates that no significant vasodilation occurred. Therefore, the decrease in blood pressure seen after ITS administration for labor analgesia is unlikely to be the result of a sympathectomy. (Key words: Analgesics, opioid: sufentanil. Anesthesia, obstetric. Anesthe-

tic techniques: intrathecal. Sympathetic nervous system: sensory changes; blood pressure changes.)

INTRATHECAL sufentanil (ITS) is frequently used to provide analgesia during labor. Decreases in blood pressure and sensory changes in this circumstance suggest that ITS may have a local anesthetic effect and thus cause a sympathetic block.¹ Fentanyl and sufentanil have been shown to decrease nerve conduction *in vitro* when given at very high concentrations.^{2,3} However, blood pressure does not decrease after ITS is given to male volunteers⁴ or when intrathecal fentanyl is given to nonlaboring women.⁵ This suggests that the blood pressure decreases after ITS in laboring women may be due to pain relief and not to a sympathectomy.

To determine whether ITS causes a sympathectomy in laboring women, we evaluated changes in toe temperature relative to calf temperature. In a nonexercising person experiencing an average environmental temperature, normal sympathetic tone causes baseline vasoconstriction of the arterioles supplying the toes. This vasoconstriction creates a temperature gradient from the toes to the central core. A sympathectomy will cause vasodilation of the arterioles secondary to loss of baseline sympathetic tone. Vasodilation will warm the toes⁶ and core body temperature will decrease secondary to the redistribution of heat.^{7,8} We compared findings in laboring women receiving ITS with those in a control group of women having spinal anesthesia with bupivacaine for elective cesarean section in whom a sympathectomy was expected secondary to the local anesthetic block.

Methods

Twenty parturients classified as American Society of Anesthesiologists' physical status 1 or 2 were enrolled in this Human Subjects Committee-approved study after giving written informed consent. Participants with diabetes or pregnancy-induced hypertension were ex-

* Assistant Professor of Anesthesia.

† Fellow in Obstetric Anesthesia.

‡ Professor of Anesthesia.

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Address reprint requests to Dr. Riley: Department of Anesthesia, Stanford University School of Medicine, Stanford, CA 94305. Address electronic mail to: edriley@Leland.Stanford.edu

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cluded. All participants had temperature probes placed on their right great toe and the lateral aspect of the mid-calf before induction of anesthesia. Central temperature was measured with a tympanic or rectal probe. The following data were recorded at the time of injection and 5, 10, 15, 20, 30, 45, and 60 min after injection: temperature at all three sites, verbal pain scores (0–10 scale where 0 = no pain and 10 = worst pain experienced), systolic blood pressure (SBP), sensory changes to temperature and pin prick, and motor block using the Bromage scale (where 0 = no block and 3 = complete block). The most recent blood pressure from the patient's clinic chart was used as the prenatal blood pressure.

Ten women in the sufentanil group (SUF) received 10 μ g ITS for labor analgesia *via* a combined spinal epidural technique using a 24- or 26-gauge pencil-point needle introduced through an 18-gauge Tuohy needle. After withdrawal of the spinal needle, an epidural catheter was threaded for later use. No local anesthetics were given *via* the needle or catheter during the study period. All SUF patients received a 1-l bolus of lactated Ringer's solution at room temperature before their blocks.

Ten women in the control group (BUP) received 12 mg hyperbaric bupivacaine, 200 μ g morphine, and 10 μ g fentanyl in their spinal anesthetics for elective cesarean section. These patients received a 2-l bolus of room temperature lactated Ringer's solution before their block and 10 mg ephedrine intravenously immediately after induction of spinal anesthesia.

Calf-to-toe temperature indices (C-T) were calculated by subtracting toe temperature from calf temperature. Toe temperature is very sensitive to vasodilation compared with calf temperature, which is more constant. Thus a decrease in this index means that the toe has warmed relative to the calf and is an indication of vasodilation.⁶ If toe temperature was not at least 4°C cooler than the calf before induction of anesthesia, this indicated that there was already some baseline vasodilation of the arterioles supplying the toes. In this circumstance, induction of a sympathectomy may not cause the toes to warm further. Therefore, these persons were excluded from the study.

Data were analyzed using paired and unpaired Student's *t* test with repeated-measures analysis of variance for repeated measurements over time. The Bonferroni correction for multiple comparisons was used, with *P* < 0.05 considered significant.

Table 1. Demographic Data

	Bupivacaine (n = 10)	Sufentanil (n = 10)
Weight (kg)	74 \pm 14	74 \pm 24
Height (cm)	167 \pm 6	164 \pm 6
Age (yr)	33 \pm 5	28 \pm 6
Gestation (wk)	38 \pm 2	40 \pm 1

Values are mean \pm SD.

Results

Patients in both groups were similar demographically (table 1). All had excellent pain control. Patients in the SUF group started with a mean verbal pain score of 6 \pm 2, and all attained verbal pain scores of 0 within 10 min of ITS administration. Patients in the BUP group reported verbal pain scores of 0 throughout their cesarean sections. In addition, all patients in both groups experienced decreased sensation to temperature. The upper dermatomal level of the change in temperature ranged from T8–T1 for the SUF group and from T1–C4 for the BUP group. All patients in the BUP group experienced a block to pin prick, with the upper level ranging from T2–C5. In the SUF group, 8 (80%) patients had decreased pin-prick sensation, with the upper level ranging from T11–T3. Bromage scores were always 0 in the SUF group and 3 in the BUP group.

There were no significant changes from baseline in central or toe temperature or C-T index in the SUF patients (fig. 1). There was a slight, transient increase in calf temperature in the SUF patients that was statistically significant but clinically insignificant (fig. 1). The BUP group had no change in calf temperature, a significant increase in toe temperature, and a corresponding decrease of the C-T index and central temperature (fig. 1).

Systolic blood pressure decreased significantly from baseline in both the SUF and BUP groups (fig. 2). However, the groups did not differ in this respect. The groups did differ in the amount of ephedrine administered. No patient in the SUF group received ephedrine, whereas all the BUP patients received ephedrine (average dose, 26 \pm 17 mg). When compared with the prenatal blood pressure obtained from the patient's chart, there was a significant increase in baseline (before block) SBP and a significant decrease in the lowest SBP recorded after induction of anesthesia in the BUP group (fig. 2). In the SUF group, there were no significant

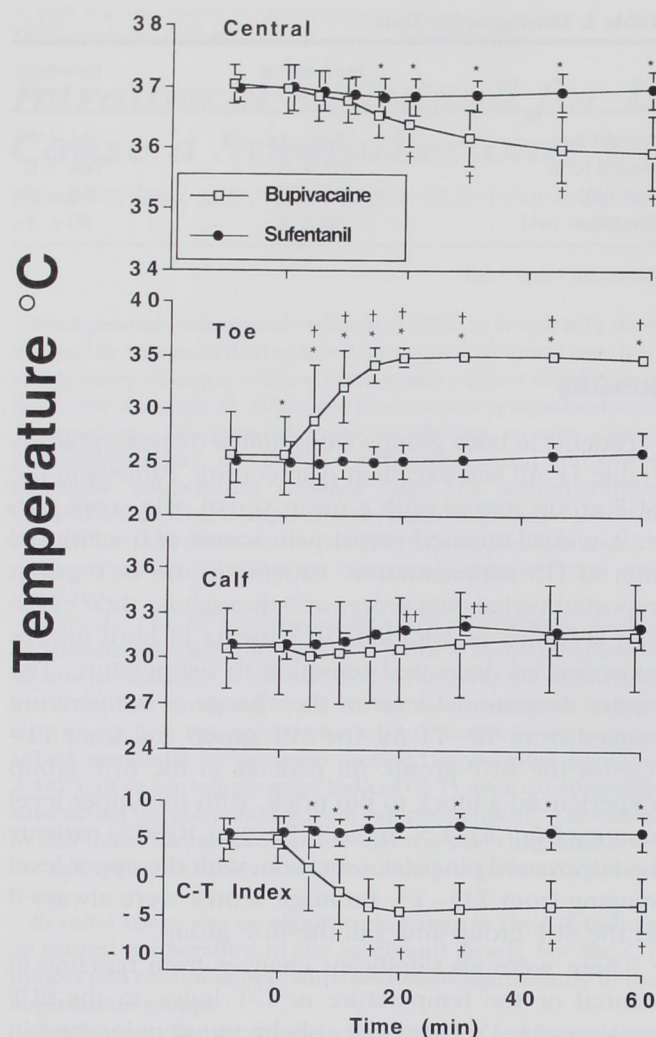


Fig. 1. Changes in central, toe, and calf temperatures and calf-to-toe index (calf temperature – toe temperature) in women after receiving either 10 μ g intrathecal sufentanil or 12 mg bupivacaine plus 10 μ g fentanyl plus 200 μ g morphine (bupivacaine). Repeated-measures analysis of variance confirmed a difference between groups over time at every site except for calf temperature. Individual time comparisons were made at 20 and 45 min using a Student's *t* test with Bonferroni's correction for multiple comparisons (*significant difference between groups; †significant difference versus baseline in the bupivacaine group; ††significant difference versus baseline in the sufentanil group with no difference between groups; $P \leq 0.05$).

differences between the prenatal SBP and either the baseline or the lowest postanesthetic SBP (fig. 2).

Discussion

All of the patients in the BUP group experienced a profound sympathetic block according to the parame-

ters measured. The decreases in the C-T index and central temperature in the BUP group were likely caused by redistribution of heat from the body core to the periphery as a result of a vasodilation.^{7,8} In the absence of core body warming, the most likely cause of vasodilation is a sympathectomy caused by intrathecal bupivacaine (there was a decrease in core body temperature in the patients in the BUP group). This would be expected with the dense blocks resulting from surgical doses of spinally administered local anesthetics. In addition, there were significant decreases in blood pressure that frequently required pressor support; profound changes to pin prick and temperature sensation; and a complete motor block in every patient.

The absence of change in the C-T indices and central temperature in the SUF group indicates that clinically significant vasodilation did not occur. Given that all these patients had some baseline vasoconstriction (baseline C-T indices $> 4^{\circ}\text{C}$), if there had been a block of sympathetic tone induced by the intrathecal sufentanil, then there would have been dilation of the arterioles supplying the toes and subsequent warming. Therefore, the decrease in blood pressure that occurs after ITS administration during labor is unlikely to be the result of a sympathectomy and is probably due to pain

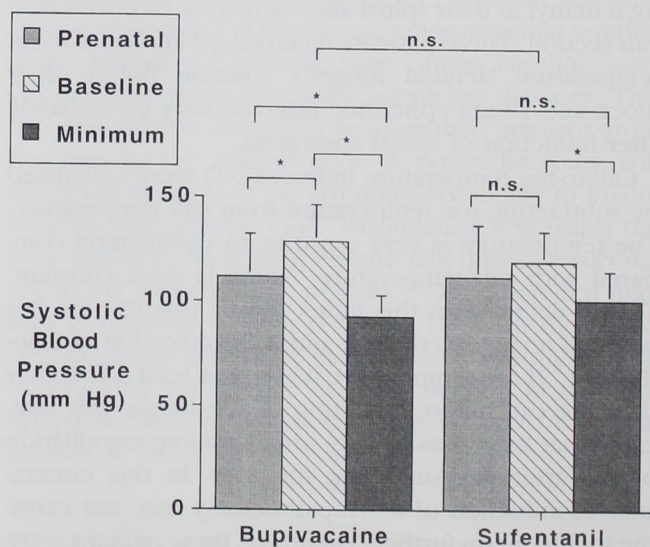


Fig. 2. Systolic blood pressure changes in women receiving either 10 μ g intrathecal sufentanil or 12 mg intrathecal bupivacaine plus 10 μ g fentanyl plus 200 μ g morphine (bupivacaine). Prenatal blood pressures were taken from the patient's last clinic visit; baseline blood pressure is the last blood pressure measured before anesthetic induction; and minimum pressure is the lowest blood pressure measured after anesthetic induction (* $P \leq 0.05$).

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relief. In support of these findings, Mandell *et al.*⁹ used an impedance cardiograph and found that intrathecal fentanyl given to laboring women did not affect stroke index or preload. Both of these parameters would be expected to decrease with vasodilation.

The fact that the minimum SBP recorded after ITS administration did not differ from the prenatal blood pressure obtained from the patients' charts provides further evidence to suggest that hypotension in this circumstance is due to pain relief and not to a sympathectomy. The baseline SBP before ITS probably was elevated secondary to pain, and the resulting pain relief returned SBP to prelabor levels. Similar results have been reported by other investigators^{10,11} when they measured blood pressure changes from prenatal values (rather than values in labor before analgesia) and compared them with values obtained after intrathecal opioids were administered. Other evidence that intrathecal opioids do not decrease blood pressure compared with nonlaboring blood pressure comes from a study by Moses *et al.*⁵ in which they administered intrathecal fentanyl to nonlaboring pregnant women; no change in blood pressure occurred. Finally, Nagasaka and Yaksh¹² showed in an animal model that administration of intrathecal opioids did not decrease control blood pressure but did prevent blood pressure increases after subjecting rats to painful stimuli.

In the BUP group, SBP after induction of spinal anesthesia was significantly lower than prenatal baseline values. This supports the theory that these patients experienced a profound sympathectomy. The significant increase in SBP from prenatal to baseline values before induction of spinal anesthesia may be due to preoperative anxiety or to the 2-l fluid load these patients received. It is surprising that the SUF patients had a lesser increase in SBP given that they were all having painful contractions. Perhaps preoperative anxiety is a more potent sympathetic stimulus than the anxiety or pain experienced during early labor. In addition, the SUF patients received a smaller fluid load (1 l vs. 2 l).

Our study could be criticized because the two study groups were quite different (comparing women having elective cesarean sections and those in labor). For instance, all the BUP patients received oxytocin after delivery. This drug can cause vasodilation. However, the patients received the oxytocin toward the end of the study period and the vasodilation we measured had occurred before its administration. The other differences between these groups would tend to promote vasoconstriction of the extremities in the cesarean sec-

tion group and vasodilation of the extremities in the laboring group. The patients having cesarean section had a larger fluid load with room temperature fluids and the abdomen was exposed and prepared with room temperature solutions. Both of these factors would tend to lower the body temperature and lead to vasoconstriction in the extremities to preserve body heat. The patients having cesarean section also received prophylactic ephedrine. This would also tend to favor vasoconstriction in the extremities because of the indirect α_1 -agonist properties of this drug. In addition, labor is "work" and generates metabolic heat. An increase in core body temperature elicits vasodilation to dissipate this heat. Therefore, laboring women should tend to have vasodilation during labor. Because we observed vasodilation in the cesarean section (BUP) group and no change in the laboring (SUF) group, we believe that it is most likely that intrathecal bupivacaine causes a sympathectomy and intrathecal sufentanil does not cause a clinically significant sympathectomy at the dose studied.

Another potential flaw in our study is that we could not control room temperature and measure temperature at as many sites as is usually done in a temperature physiology laboratory. However, we do not believe this affected our results. Rather than trying to do careful heat budgets of the body, we used temperature changes in the extremities as a marker of vasodilation in a clinical setting. The temperature shifts we were expecting were of greater magnitude and would happen much faster than changes due to small differences in room temperature or minor shifts in regional blood flow.

The fact that the SUF patients did not develop a clinically evident sympathectomy or any evidence of a motor block suggests that intrathecal sufentanil does not act as a local anesthetic at the doses given. In support of this hypothesis, Jaffe and Rowe¹³ have shown that sufentanil and fentanyl, at clinically relevant concentrations, do not affect nerve conduction in isolated dorsal root axons. However, if intrathecal sufentanil does not have local anesthetic properties, how can we explain the observed sensory changes? Wang *et al.*¹⁴ have shown in an animal model that intrathecal opioids block the afferent limb of the sympathetic nervous system (A-delta and C-fiber input) but not the efferent limb. This suggests that the sensory changes are not caused by opioids interacting with sodium channels on nerve axons but rather are caused by an interaction with opioid receptors in the spinal cord.

Although blood pressure changes after intrathecal su-

fentanyl do not appear to be due to a sympathectomy and may merely be a return to normal prelabor values, this does not mean that they have no clinical significance. Fetal heart rate changes¹ and profound fetal bradycardia¹⁵ have been reported after intrathecal sufentanil and fentanyl administration. These events may be due to an increase in uterine tone resulting from the rapid onset of analgesia. Because β -adrenergic stimuli have a tocolytic effect, a sudden decrease in circulating catecholamines after the onset of pain relief may result in disinhibition of uterine contractility and therefore uterine hypertonus. Alternatively, a relatively rapid decrease in blood pressure, similarly arising from an acute decrease in circulating catecholamines, could cause impaired perfusion of the placenta and result in the fetal heart rate changes observed.

In summary, we found that intrathecal sufentanil does not cause a clinically significant sympathectomy. The blood pressure decreases observed after intrathecal sufentanil administration are most likely due to pain relief. The sensory changes seen after intrathecal sufentanil are probably due to an opioid interaction with the afferent limb of the sympathetic nervous system.

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